

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2005/000774

International filing date (day/month/year)
28.02.2005

Priority date (day/month/year)
26.02.2004

International Patent Classification (IPC) or both national classification and IPC
C12Q1/70

Applicant
NORCHIP AS

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Bellmann, A

Telephone No. +31 70 340-8958



10/590678


**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/GB2005/000774**IAP5 Rec'd PCT/PTO 25 AUG 2006****Box No. I Basis of the opinion**

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:


**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/GB2005/000774

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
Industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	4-12
	No: Claims	1-3
Inventive step (IS)	Yes: Claims	-
	No: Claims	1-12
Industrial applicability (IA)	Yes: Claims	1-12
	No: Claims	-

2. Citations and explanations

see separate sheet



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2005/000774

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

The following documents are referred to in this communication:

- D1: WO 03/057914 A (NORCHIP A/S; KARLSEN, FRANK; ALLARD, SUSAN, JOYCE) 17 July 2003 (2003-07-17)
- D2: LANHAM S ET AL: "HPV detection and measurement of HPV 6, telomerase and survivin transcripts in colposcopy clinic patients" JOURNAL OF CLINICAL PATHOLOGY, LONDON, GB, vol. 54, no. 4, April 2001 (2001-04), pages 304-308, XP002961294 ISSN: 0021-9746
- D3: SMITS H L ET AL: "APPLICATION OF THE NASBA NUCLEIC ACID AMPLIFICATION METHOD FOR THE DETECTION OF HUMAN PAPILLOMAVIRUS TYPE 16 E6-E7 TRANSCRIPTS" JOURNAL OF VIROLOGICAL METHODS, AMSTERDAM, NL, vol. 54, no. 1, 1995, pages 75-81, XP009015131 ISSN: 0166-0934

1 NOVELTY (Article 33(2) PCT)

- 1.1 An *in vitro* method of screening human subjects for the presence of human papillomavirus in at least one cell or tissue, wherein the human papillomavirus exhibits loss of regulation of E6/E7 mRNA expression and loss of replication and/or expresses a stabilized pre-mRNA encoding full length E6 protein, the method comprising detecting the presence of mRNA transcripts of the E6/E7 gene of a human papilloma virus which encode full length E6 protein in a test sample comprising mRNA derived from the cell or tissue, wherein the presence of such E6/E7 mRNA transcripts in the sample is taken as an indication of the presence of human papillomavirus exhibiting loss of regulation of E6/E7 mRNA expression and loss of replication and/or expresses a stabilized pre-mRNA encoding full length E6 protein in the cell or tissue, is disclosed in D1 (cf. p.6 to 9, p.21 to 23, p.26, par.3, p.31, par.1 and 2, cl.1,2,6), D2 (cf. p.3, col.2, par.3, p.4 and Tab.2) and D3 (cf. whole document).



**WRITTEN OPINION OF THE
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International application No.

PCT/GB2005/000774

Therefore, the subject-matter of **independent claim 1 is not novel over D1 to D3** (Article 33(2) PCT).

- 1.2 D1 discloses also an *in vitro* method of screening human subjects for the presence cellular changes characterized by enlarged cell nuclei and cellular aneuploidy in at least one cell or tissue, which method comprises detecting the presence of mRNA transcripts of the E6/E7 gene of a human papilloma virus which encode full length E6 protein in a test sample comprising mRNA derived from the cell or tissue, wherein the presence of such E6/E7 mRNA transcripts in the sample is taken as an indication that the cell or tissue under test exhibits the cellular changes (cf. D1, p.6 to 9, p.21 to 23, p.26, par.3, p.31, par.1 and 2, cl.7).

Therefore, the subject-matter of **independent claim 2 is not novel over D1** (Article 33(2) PCT).

- 1.3 D1 discloses furthermore an *in vitro* method of screening human subjects for the presence of persistent transforming infection with human papillomavirus in at least one cell or tissue, which method comprises screening the subject for expression of mRNA transcripts of the E6/E7 gene of a human papilloma virus which encode full length E6 protein in a test sample comprising mRNA derived from the cell or tissue, wherein subjects positive for expression of such mRNA transcripts of the E6/E7 gene of human papillomavirus are scored as having a persistent transforming infection with human papillomavirus in the one cell or tissue (cf. D1, p.6 to 9, p.11, p.21 to 23, p.26, par.3, p.31, par.1 and 2, cl.1,2,6).

Therefore, the subject-matter of **independent claim 3 is not novel over D1** (Article 33(2) PCT).

2 INVENTIVE STEP (Article 33(3) PCT)

- 2.1 Dependent claims 4 to 12 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, as all of the additional features fall within the scope of routine laboratory practise.